Customer No. 00270

GGP2CUSA

REMARKS

Applicant Gideon Goldstein and the undersigned attorney express their appreciation to Examiner Parkin for the courtesy of the telephone interview conducted on October 8, 2003, and for the Interview Summary Sheet dated October 9, 2003. The pending claims are 1-10. Claim 1 has been amended for clarification, and this amendment is supported throughout the specification. No new matter is added by this amendment.

Applicant's Invention

In contrast to HIV-1 antibodies of the prior art, Applicant's invention as embodied in the pending claims is not simply a composition, which contains an antibody directed to only a Tat protein from a single HIV-1 strain or subtype. Rather, Applicant's invention is based upon the recognition that a particular epitope sequence varies among multiple different strains and subtypes of HIV-1. The composition is such that at least one antibody binds *at least two* variants of the epitope, thereby allowing the antibody composition to bind to multiple different HIV-1 strains and subtypes. The epitope in question is located within the amino acid sequence of Epitope I SEQ ID NO: 36. The optional addition of antibodies that bind to other epitopes, e.g., an epitope located within the amino acid sequence of Epitope II peptide (claim 4), can increase the efficacy of the compositions.

The claims precisely define antibodies that bind an epitope located within the amino acid sequence of SEQ ID NO: 36, wherein the epitope varies at amino acid position Y. The antibody composition binds to HIV-1 Tat proteins from different HIV-1 strains and subtypes. The epitope sequence of SEQ ID NO: 36 comprises amino acid residues 4 -10 of the HIV-1 Tat protein SEQ ID NO: 1. This description of the antibodies suitable for inclusion in such a composition is fully supported in the specification in Examples 7 and 9, and in the specification pages 28-29 and 45-53, among other portions of the specification. This clarification of the epitope description further distinguishes the antibodies claimed by Applicant from other HIV-1 antibodies known to those of skill in the art.

While the examiner did not cite any prior art discussing HIV-1 Tat antibodies, Applicant makes the following brief statement as requested by the examiner during the above-noted interview. To Applicant's knowledge, prior art HIV-1 antibodies were generated to the same HIV-1 Tat sequence, from strains HXB2 or LAV, in which the "Y" amino acid in Applicant's identified epitope was only Arg. Thus, any antibodies developed to the Tat sequence from that strain would not bind "at least two variants" of Applicant's identified epitope. To Applicant's knowledge, no one of skill in the art has been motivated to make or use a composition containing at least one antibody that binds to at least two variants (i.e. at least 2 different amino acids in position "Y") of the specifically claimed Tat epitope. Nor does the prior art teach combining in a composition antibodies that bind additional Tat sequences (e.g., Claim 4).

For example, references cited in a related application as disclosing HIV-1 antibodies of the art included Hinkula *et al*, 1997 *J. Virol., 71*(7):5528-5539 and G. R. Pilkington *et al*, 1996 *Mol. Immunol., 33*(4/5):439-450. Neither document discloses an antibody composition as defined by Applicant, said antibody composition reacting with HIV-1 Tat proteins from different HIV-1 strains and subtypes. Both Hinkula and Pilkington refer to antibodies or antibody fragments raised to the HXB2 strain of HIV-1. This strain contains an Arg at the "Y" variant of the sequence of claim 1.

Hinkula elicited a polyclonal immune response by immunizing mice with *either* a plasmid containing the ***entire*** HIV-1 *tat* gene of strain HXB2 under the control of the HCMV IE promoter (see col. 2, p. 5528) or an ***entire*** recombinant Tat protein (see col. 1, p. 5529). Hinkula specifically identifies binding to two epitopes, each within a 20 amino acid sequence. One of these antibodies is described as binding to an epitope within aa residues 1-20 of Tat for mouse anti-rTat response (page 5533, the lines spanning cols. 1 and 2 under the Fig. 2). However, because Hinkula's antibody was raised to the single "Y" variant sequence of HIV-1 Tat of HXB2, this antibody does not cross-react with multiple different HIV-1 Tat variants, as described by Applicant. No interpretation of Hinkula's data suggests an antibody composition as defined by claim 1.

Similarly, Pilkington refers to human antibody fragments produced by panning a human Fab phage display library of PBLs from an asymptomatic HIV-1 infected patient. This patient was infected with the HXB2 strain. Pilkington states that the Fab were directed to the functional domain found between aa 22-33 of Tat, an epitope completely ***outside*** of the epitope to which Applicant's antibodies bind and having a completely different amino acid sequence. No interpretation of Pilkington's data suggests an antibody composition as defined by claim 1.

Only Applicant has taught (see page 55-56 of the specification) antibody compositions comprising antibodies that bind specifically to at least two variants within the amino acid epitope SEQ ID NO: 36. Only Applicant has described that such cross-reactive antibody compositions are capable of reacting with 96% of known HIV-1 Tat strains and subtypes. To Applicant's knowledge, no antibodies of the prior art that are raised to and bind an HIV-Tat sequence from the single HIV-1 strain HXB2 may be characterized as binding multiple different HIV-1 strains and subtypes.

35 USC § 112, First Paragraph Rejection

> The Examiner has rejected claims 1-10 under 35 USC § 112, first paragraph and has asserted that the claims fail to provide any details pertaining to the structure of any given antibody, that the disclosure fails to provide any information pertaining to the molecular determinants modulating the antibody-antigen binding interaction, and that the specification is silent pertaining to the structure details of the polyclonal, monoclonal, chimeric, humanized, human and phage display antibodies.

As discussed in the above-noted telephone conference, the identification of the epitope to which an antibody binds is a key structural and functional characteristic of an antibody. See also, the portions of the specification cited above for support of the claimed subject matter. The Examiner agreed during the telephone conference and acknowledged in the Interview Summary the withdrawal of this rejection.

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In view of the above amendments, remarks and the Interview Summary, Applicant requests that the pending claims be found allowable and this application proceed to issuance in due course.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,

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